Program/Abstract # 164
vgl-2a is required for endodermal pouch morphogenesis in zebrafish craniofacial development
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The development of the vertebrate cranial skeleton results from the specification, growth, patterning, and morphogenesis of tissues derived from all three germ layers in response to a complex network of reciprocal signaling. While many genes involved in these processes have been identified, additional novel genes involved in craniofacial development remain uncharacterized. We have identified a gene, *vgl-2a*, which is expressed in the pharyngeal endoderm and ectoderm surrounding the neural crest derived mesnechyme of the pharyngeal arches in zebrafish. We have found that reducing expression of *vgl-2a* in zebrafish embryos using morpholino injection results in a loss of cranial cartilages, demonstrating a previously undescribed requirement for *vgl-2a* in craniofacial development. Inhibiting FGF signaling results in reduced expression of *vgl-2a* within the region of the pharyngeal arches, suggesting that FGF signaling is required for *vgl-2a* expression in these cell populations. We have also demonstrated that reducing expression of *vgl-2a* results in a defect in endodermal pouch morphogenesis, a process that has been shown to require FGF signaling and that is essential for later development of the pharyngeal skeleton.

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Program/Abstract # 165
Wnt signals facilitate behavioral transitions during zebrafish pancreas morphogenesis
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We are developing a quantitative model of zebrafish pancreas development utilizing live and static confocal imaging of novel transgenic embryos coupled with computer-assisted analyses. We show that Pancreatic Progenitor Cells (PPCs) are mostly specified on the left side of the foregut at ~32 hpf after which they grow and spread across the midline towards the islet. Live imaging of nuclear-targeted fluorescent transgenic lines demonstrates that individual cells within the cluster move in random directions during migration. Following aggregation, which takes about 8 h, PPCs change direction and extend posteriorly. We are quantifying aspects of this relatively simple series of transformations under normal and perturbed conditions to classify PPC behaviors. For example, affecting different components of the Wnt pathway resulted in reduction of PPC volume, surface area and changes to spatial and temporal organizations. Moreover, the system demonstrates adaptive behavior at different stages. Combined, our morphometric analyses describe qualitative and quantitative behavioral changes operating during PPC development and implicate Wnt signals in facilitating passage through these transitions.

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Program/Abstract # 166
Zebrafish Wnt signaling co-operates with FAK in controlling slow muscle alignment along myotome boundaries
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Studies in *Xenopus* cell culture suggested that FAK may be involved in the development of the myotendious junction. However, the underlying molecular mechanism of myotendious junction development remains unclear. Here, we study the function of zebrafish Frizzled 7b (Fz7b) in muscle development in vivo during primary myogenesis using zebrafish as an animal model. We have found that Fak1a protein accumulates at the myotome junction where slow muscle fibrils are aligned parallel across the myotome. Knockdown of Fz7b reduces Focal Adhesion Kinase 1a (Fak1a) accumulation in this location and down-regulates expression of titin and related molecules. In addition, we show that knockdown of Fak1a partially phenocopies that of fz7b morphants. This work suggests that Wnt signaling is required during slow muscle morphogenesis and correlates to the role of Fak1a in the proper alignment of slow fibrils. Moreover, a slight decrease in the level of Fak1a dramatically increases the morphogenetic defect in the n-cadherin/parachute mutant, indicating that these two systems interact to control slow twitch muscle attachment. Interestingly, our data further reveal that zebrafish wnt5/pipetail and disheveled3 are also required for Fak1a accumulation at the junctions of myotome as well as slow muscle attachment during migration. These results provide the first example of focal adhesion cooperation with Wnt pathway in vertebrate slow muscle development and imply that Fak cooperation with Wnt signaling could be a widespread phenomenon and conserved pathway.

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Program/Abstract # 167
Regulation of cardiac morphogenesis in zebrafish by hand2
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The bHLH transcription factors Hand1 and Hand2 were identified as essential regulators of heart development more than a decade ago. Despite their prominent and conserved roles, how Hand factors control cardiac morphogenesis is still unknown. In zebrafish, mutation of *hand2* causes a striking cardiac phenotype. Instead of having normal bilateral populations of cells that migrate to form a heart tube at the midline, *hand2* mutants maintain two separated populations of cells that never fuse. Normal cardiac fusion requires the formation of a myocardial epithelium possessing apicobasal polarity. In *hand2* mutants, the cardiomyocytes do not form an epithelium, show misplacement of polarization markers, and display aberrant fibronectin deposition. Through gene expression profiling, we identify several transcripts that are differentially regulated in *hand2* mutants and may be fundamental for cardiac fusion. For example, the genes encoding the ligand-receptor pair *fibronectin1* (*fn1*) and *integrin*-α5 (*itga5*) appear upregulated in *hand2* mutants. Moreover, overexpression of *hand2* results in a cardiac phenotype similar to that of *fn1* mutants. Together, our data suggest a model in which Hand2 regulates cardiac fusion by modulating expression of *fn1* and *itga5*.

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